



NDA 20-010

Schering-Plough Research Institute
Attention: Joseph F. Lamendola, Ph.D.
Vice President, U.S. Regulatory Affairs
2000 Galloping Hill Road
K-6-1/1345
Kenilworth, New Jersey 07033

Dear Dr. Lamendola:

Please refer to your new drug application (NDA) dated August 31, 1989, received September 5, 1989, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Lotrisone (clotrimazole and betamethasone dipropionate) Lotion.

Please also refer to our Not Approvable letters dated June 29, and December 31, 1990, and our Approvable Letter dated July 31, 1991.

We acknowledge receipt of your submissions dated August 6 and 30 and September 16, 1991; March 26 and May 6, 1992; June 6, August 25, September 16, October 20 and 21 (2) and December 1 and 14, 1994; January 5, October 7 and 26, 1999; March 3 (3), 7 and 13, April 5 (2), and 13 (2), May 5 and 10, June 8, 21 and June 30, July 13, 21 and 27, August 2, 15, 16 and 30, September 27 and 29, October 13, November 29 and December 6, 2000 (facsimile). Your submission of October 7, 1999, constituted a complete response to our July 31, 1991, action letter.

This new drug application provides for the use of Lotrisone (clotrimazole and betamethasone dipropionate) Lotion for the topical treatment of symptomatic inflammatory tinea pedis, tinea cruris, and tinea corporis due to *Epidermophyton floccosum*, *Trichophyton mentagrophytes*, and *Trichophyton rubrum*.

We have completed the review of this application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon enclosed labeling text. Accordingly, the application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert, text for the patient package insert, immediate container and carton labels). Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit 20 paper copies of the FPL as soon as it is available, in no case more than 30 days after it is printed.

Please individually mount ten of the copies on heavy-weight paper or similar material.

Alternatively, you may submit the FPL electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDAs* (January 1999). For administrative purposes, this submission should be designated "FPL for approved NDA 20-010." Approval of this submission by FDA is not required before the labeling is used.

We remind you of your post marketing commitment specified in your submission dated December 6, 2000 (facsimile). This commitment, along with completion date agreed upon, is listed below.

Evaluate the efficacy of Schering's educational campaign by monitoring the pediatric use of Lotrisone Lotion and Lotrisone Cream in age groups: 0-1, 1-2, 2-4, 4-8, and 8-12 years for; 1) all uses and 2) uses in diaper dermatitis. Usage will be estimated by utilizing the IMS Health databases; physician survey data from the National Disease and Therapeutic Index (NDTI) should be used to estimate the percentage of total use in these specified populations then multiplied by the total Lotrisone usage available through the National Prescription Audit (NPA) to derive the estimated Lotrisone use in the above specified age groups. A second database, estimating prescription use through any means in the above populations, will be utilized to support the IMS estimate. Such evaluations are to be performed annually. A baseline evaluation, i.e., before the labeling change (e.g., 1999 or 2000) should be submitted within three months of approval.

Protocols, data, and final reports should be submitted to your IND for this product and a copy of the cover letter sent to this NDA. If an IND is not required to meet your post marketing commitments, please submit protocols, data and final reports to this NDA as correspondence. In addition, under 21CFR 314.81(b)(2)(vii), we request that you include a status summary of each commitment in your annual report to this NDA. The status summary should include the number of patients entered in each study, expected completion and submission dates, and any changes in plans since the last annual report. For administrative purposes, all submissions, including labeling supplements, relating to these post marketing commitments must be clearly designated "Post Marketing Commitments."

Validation of the regulatory methods has not been completed. At the present time, it is the policy of the Center not to withhold approval because the methods are being validated. Nevertheless, we expect your continued cooperation to resolve any problems that may be identified.

Be advised that, as of April 1, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (63 FR 66632). We note that you have not fulfilled the requirements of 21 CFR 314.55. We are deferring submission of your final pediatric study reports between the ages of 12 and 17 years until December 31, 2002. We are waiving pediatric studies below the age of 12 years under 21 CFR 314.55(c)(4), because the use of Lotrisone Cream and Lotion is not recommended in patients below the age of 12 years. However, in the interim, please submit your pediatric drug development plans within 120 days from the date of this letter. Within approximately 120 days of receipt of your pediatric drug development plan, we will review your plan and notify you of its adequacy.

Pediatric studies conducted under the terms of section 505A of the Federal Food, Drug, and Cosmetic Act may result in additional marketing exclusivity for certain products (pediatric exclusivity).

You should refer to the *Guidance for Industry on Qualifying for Pediatric Exclusivity* (available on our web site at www.fda.gov/cder/pediatric) for details.

If you wish to qualify for pediatric exclusivity you should submit a "Proposed Pediatric Study Request" (PPSR) in addition to your plans for pediatric drug development described above. We recommend that you submit a Proposed Pediatric Study Request within 120 days from the date of this letter. If you are unable to meet this time frame but are interested in pediatric exclusivity, please notify the division in writing. FDA generally will not accept studies submitted to an NDA before issuance of a Written Request as responsive to a Written Request. Sponsors should obtain a Written Request before submitting pediatric studies to an NDA. If you do not submit a PPSR or indicate that you are interested in pediatric exclusivity, we will review your pediatric drug development plan and notify you of its adequacy. Please note that satisfaction of the requirements in 21CFR 314.55 alone may not qualify you for pediatric exclusivity. FDA does not necessarily ask a sponsor to complete the same scope of studies to qualify for pediatric exclusivity as it does to fulfill the requirements of the pediatric rule.

In addition, please submit three copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please submit one copy to this Division and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

Please submit one market package of the drug product when it is available.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, please call Frank H. Cross, Jr., M.A., CDR, Senior Regulatory Management Officer, at (301) 827-2020.

Sincerely,

Jonathan K. Wilkin, M.D.
Director
Division of Dermatologic and Dental Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research

Enclosure

APPEARS THIS WAY
ON ORIGINAL